

WHAT IS CLAIMED IS:

1. A method of detecting virus binding and entry to target cell, said method comprises the steps of:

5 attaching an enzyme to the C-terminal end of a viral envelope protein, thereby creating an envelope-enzyme fusion protein;

generating virus particles comprising said fusion protein and wild type viral envelope protein;

10 infecting target cells with said virus particles; and

measuring activities of said enzyme in said infected cells, wherein said enzyme activities are measures of virus binding and entry to said target cells mediated by said wild type viral envelope protein.

15 2. The method of claim 1, wherein said enzyme is luciferase.

3. The method of claim 1, wherein said fusion protein comprises envelope protein of murine leukemia virus.

20 4. The method of claim 1, wherein said wild type viral envelope protein is from a virus selected from the group consisting of murine leukemia virus, human immunodeficiency virus, retrovirus, Vesicular Stomatitis virus, Arenaviruses, Hanta virus, Ebola virus and Venezuelan Equine Encephalitis virus.

25 5. The method of claim 1, wherein said measurement of enzyme activities is carried out in 96-well plate.

6. A method of evaluating influence of amino acid substitutions on virus binding and entry, said method comprises the steps of:

constructing a mutant containing the amino acid substitution in
5 the viral envelope protein,

attaching an enzyme to the C-terminal end of mutant viral envelope protein, thereby creating a mutant envelope-enzyme fusion protein;

generating virus particles comprising of said mutant fusion protein and wild type viral envelope protein;

10 infecting target cells with said virus particles; and

measuring the activities of said enzyme in said lysed and intact infected cells, thereby evaluating the influence of amino acid substitutions on virus binding and entry.

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7. The method of claim 6, wherein the said enzyme is luciferase.

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8. The method of claim 6, wherein said mutant fusion protein comprises envelope protein of murine leukemia virus.

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9. The method of claim 6, wherein said wild type viral envelope protein is from a virus selected from the group consisting of murine leukemia virus, human immunodeficiency virus, retrovirus, Vesicular Stomatitis virus, Arenaviruses, Hanta virus, Ebola virus and Venezuelan Equine Encephalitis virus.

10. The method of claim 6, wherein said measurement of enzyme activities is carried out in 96-well plate.

5 11. A method for determining whether the mechanism of viral entry is dependent on pH, said method comprises the steps of:

attaching an enzyme to the C-terminal end of a viral envelope protein, thereby creating an envelope-enzyme fusion protein;

10 generating virus particles comprising of said fusion protein and wild type viral envelope protein;

infecting target cells with said virus particles; and

15 measuring the activities of said enzyme in said infected cells in the presence and absence of inhibitors of endosomal acidification, wherein decreased enzyme activities in the presence of the said inhibitors indicates that the virus has a pH-dependent mode of entry.

12. The method of claim 11, wherein the said enzyme is luciferase.

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13. The method of claim 11, wherein said fusion protein comprises envelope protein of murine leukemia virus.

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14. The method of claim 11, wherein said wild type viral envelope protein is from a virus selected from the group consisting of murine leukemia virus, human immunodeficiency virus, retrovirus, Vesicular Stomatitis virus, Arenaviruses, Hanta virus, Ebola virus and Venezuelan Equine
30 Encephalitis virus.

15. The method of claim 11, wherein said measurement of enzyme activities is carried out in 96-well plate.

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16. A method of receptor-dependent targeted therapy to an individual, said method comprises the step of:

attaching a therapeutic protein to the C-terminal end of a viral envelope protein, thereby creating fusion protein;

10 generating virus particles comprising said fusion protein and wild type viral envelope protein;

administering said composition to an individual, wherein said administration mediates receptor-dependent targeted therapy to said individual.

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17. The method of claim 16, wherein said fusion protein comprises envelope protein of murine leukemia virus.

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18. The method of claim 11, wherein said wild type viral envelope protein is from a virus selected from the group consisting of murine leukemia virus, human immunodeficiency virus, retrovirus, Vesicular Stomatitis virus, Arenaviruses, Hanta virus, Ebola virus and Venezuelan Equine
25 Encephalitis virus.

19. The method of claim 16, wherein the therapeutic protein is a toxin, a chemotherapeutic agent, an immune stimulant, cytotoxic agent or
30 attached to a radioisotope.

20. The method of claim 16, wherein the therapeutic protein may be about 61 kDa in size.

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21. A pharmaceutical composition comprising of therapeutic protein-containing virus.

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22. A pharmaceutical composition of claim 21, wherein the therapeutic protein is a toxin, a chemotherapeutic agent, an immune stimulant, cytotoxic agent or attached to a radioisotope.

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23. A pharmaceutical composition of claim 21, wherein the said virus comprises therapeutic protein fused to envelope protein of murine leukemia virus.

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24. A pharmaceutical composition of claim 21, wherein the wild type envelope protein in the said virus is from a virus selected from the group consisting of murine leukemia virus, human immunodeficiency virus, retrovirus, Vesicular Stomatitis virus, Arenaviruses, Hanta virus, Ebola virus and Venezuelan Equine Encephalitis virus.

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25. A pharmaceutical composition of claim 21, wherein the said therapeutic protein may be about 61 kDa.

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26. A method for screening neutralizing antibodies in patients' sera, said method comprises the steps of:

attaching an enzyme to the C-terminal end of viral envelope protein, thereby creating an envelope-enzyme fusion protein;

generating virus particles comprising said fusion protein and wild type viral envelope protein;

infecting target cells in the patients sera with said virus particles; and

measuring the activities of said enzyme in said infected cells of the sera, wherein decreased enzyme activities in said sera indicates that there are neutralizing antibodies in the sera.

27. The method of claim 21, wherein said enzyme is luciferase.

28. The method of claim 21, wherein said fusion protein comprises envelope protein of murine leukemia virus.

29. The method of claim 21, wherein said wild type viral envelope protein is from a virus selected from the group consisting of murine leukemia virus, human immunodeficiency virus, retrovirus, Vesicular Stomatitis virus, Arenaviruses, Hanta virus, Ebola virus and Venezuelan Equine Encephalitis virus.

30. The method of claim 21, wherein said measurement of enzyme activities is carried out in 96-well plate.

31. A diagnostic kit for screening neutralizing antibodies in patient sera, said kit comprising:

- (a) enzyme-containing virus pseudotypes
- (b) substrate for said enzyme.

32. The kit of claim 26, wherein the enzyme in the said enzyme containing virus pseudotypes is luciferase.

33. The kit of claim 26, wherein said virus pseudotypes comprise said enzyme fused to envelope protein of murine leukemia virus.

34. The kit of claim 26, wherein said virus pseudotypes comprise wild type envelope protein of a virus selected from the group consisting of murine leukemia virus, human immunodeficiency virus, retrovirus, Vesicular Stomatitis virus, Arenaviruses, Hanta virus, Ebola virus and Venezuelan Equine Encephalitis virus.

35. The kit of claim 26, wherein the said substrate is luciferin.

36. A method of screening for compound that inhibits virus binding and entry to target cell, said method comprises the steps of:

attaching an enzyme to the C-terminal end of a viral envelope protein, thereby creating an envelope-enzyme fusion protein;

generating virus particles comprising said fusion protein and wild type viral envelope protein;

infecting target cells with said virus particles in the presence or absence of said compound; and

5 measuring activities of said enzyme in said infected cells, wherein decreased enzyme activities in the presence of said compound indicates that said compound inhibits virus binding and entry to said target cells mediated by said wild type viral envelope protein.

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37. The method of claim 26, wherein said enzyme is luciferase.

15 38. The method of claim 26, wherein said envelope-enzyme fusion protein comprises envelope protein of murine leukemia virus.

20 39. The method of claim 26, wherein said wild type viral envelope protein is from a virus selected from the group consisting of murine leukemia virus, human immunodeficiency virus, retrovirus, Vesicular Stomatitis virus, Arenaviruses, Hanta virus, Ebola virus and Venezuelan Equine Encephalitis virus.

25 40. The method of claim 26, wherein said measurement of enzyme activities is carried out in 96-well plate.